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09/266,813 03/12/99 SATOH

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HM22/0605

EXAMINER

SHEINBERG, M

ART UNIT

PAPER NUMBER

1631

DATE MAILED:

06/05/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/266,813

Applicant(s)

SATOH ET AL.

Examiner

Monika B. Sheinberg

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-20 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claims ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 12 March 1999 is/are objected to by the Examiner. (See PTO-948)
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 1 sheet.

- 18) ☐ Interview Summary (PTO-413) Paper No(s) ____.
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: _____

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the *first paragraph* of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPA 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The instant application lacks any amount or direction as to the practice of the generating a useful resulting probe point or probe atom as seen in claim 1, lines 17 and 29 respectively.

Nowhere in the claims or the specification is there a clear and direct explanation as to how the stated elements are to be selected from a molecule. While working examples are not, per se, required, the specification must provide adequate guidance such that one of skill in the art could practice the invention without undue experimentation. Given the lack of working examples in the specification, and the unpredictability of the selecting an atom or a probe point in the context of a complex or simple molecule, the specification, as filed is not enabling for the method of selecting/determining atoms or points as probes as claimed. As such, claims drawn to the use of probe atoms or probe points are not enabled.

In addition, the attempt to incorporate subject matter into this application by reference to Voronoi diagram or division in AMC onputting Surveys, (vol.23, 1991 etc) on page 14, lines 18-22 is improper because the Voronoi division is essential material to functionable carry out the method steps of the instant invention. The Voronoi mathematical derivations are referenced to repeatedly throughout the specification as well as stated as an essential step in claim 8, lines 3 and 6. See the paragraph below regarding improper incorporation by reference of essential subject matter.

The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179

USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for three elements for deriving a rate, does not reasonably provide enablement for determining how they come together to create the actual "space occupied rate"(claim 1, line 20). The rate derivation was not sufficiently developed in the specification to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPA 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The three elements of which the rate is based are provided in claims 9-11: claim 9 states a basis of the rate on an undefined volume (line 2-3); claim 10 states a basis on probe points (line 3); and claim 11 states a basis of the rate on an area of said frontier surrounding space (line 3).

The scope of enablement continues to claim 12, which describes using the rate in normalizing an electrostatic factor and a steric factor. If the rate cannot be determined in itself, then the following use of the undefined derived rate cannot be used to perform the normalization calculations as described in claim 12. As such, claims drawn to the use and/or determination of the space occupied are not enabled.

The following is a quotation of the *second paragraph* of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected for lack of clarity as to how the space occupied rate provided in line 20, is derived. The specification states on page 12, lines 8-9, that the claimed rate "is given as the number of the probe points...", yet in claim 10, the rate is "based on [a] number of probe points" (line 3). The specification does not clarify the metes and bounds of these probe points in order to derive the stated rate. In addition, three elements on which the claimed space occupied rate are based on are provided in claims 9-11, yet themselves are not clearly defined either. The volume as provided in claim 9 line 3, of an unknown quantity not defined in either the claims or the specification renders the claim indefinite. The number probe points provided in claim 10, line 3, is unknown and also not defined in either the claims or the specification. The same relates to the area of the frontier surrounding surface stated in claim 11, line 3. With the three elements rendered indefinite, along with an unclear statement of which combination would render them

capable of deriving a rate, make claim 1 indefinite as well as any dependent claims. In addition, the undefined space occupied rate is utilized in claims 18-20, and thus these claims are rendered indefinite.

Claim 1 is also rejected due to the unclarity caused by a lack of clearly defined derivation steps that are set forth in lines 22-27 for deriving electrostatic energies. It is unclear as to whether the electrostatic energies are being derived between: "a unit charge set at each of said probe points" (lines 22-23) and "charges of all of atoms of said molecule" (lines 23-24); or the stated unit charge set and charges of all atoms of a corresponding one of said component spaces. The reason as to why the sum of electrostatic energies remains parameterized by each component space, contradicts the electrostatic energy derivation per unit charge set is based upon all the component spaces simultaneously. As such, the lack of clarity in deriving electrostatic energies renders claim 1 indefinite and all claims that are dependent upon claim 1, or drawn to the use of the discussed derivation (claims 18-20) are also indefinite.

Claim 1 is rejected, as having unclear language that causes a lack of clarity in what the desired meaning of a probe atom or a probe point. If a probe atom "is set at each of the said probe points" (claim 1, lines 29-30) then there exist a contradiction to "probe points [...] existing on the [...] surface of each of the atoms" (specification, page 12, lines 9-12). It is unclear if the probe atom is encompassed by the probe point; or the probe point is encompassed by the probe atom.

Claim 1 is also rejected, as having unclear language that causes a lack of clarity as to what the desired meaning of "said" atoms in line 31. Claim 1 fails to define what constitutes the atoms of the claimed molecule. It is confusing as to which atoms the specified area of the claim

refers to: either it refers to any atoms of the mentioned molecule, or it refers to the set probe atoms of the molecule.

Claim 19 is rejected, as having unclear language that causes a confusing conflict to what is desired of the claim. The conflict lies in what the claim sets out to describe: a product, the reaction characteristic prediction map; or the method of making the stated map.

Claim 20 is rejected for the lack of clarity in describing that which the preamble sets out to claim, a "storage medium" (line 1). No where in the claim is there a statement referring to the storage of any values or information. All the points, rates, energies, etc. are created or assumed yet not selected from a list, or stored to a database for later selective retrieval. Therefore, it is questionable whether it is a storage medium that is being claimed or the program that creates a means to apply the claimed methods.

Claims 4 and 5 recite the limitation "atomic spherical surfaces" in line 2 of both claims. There is insufficient antecedent basis for this limitation in the claim. Claim 4 points to claim 3, and claim 5 points to claim 1; yet, neither claim 3, nor claim 1 has introduced the limitation "atomic spherical surfaces". It is noted however, that the stated limitation is introduced in claim 2. Please make the appropriate adjustments in claim 4 and 5 to properly refer to the correct claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 1, 9-12, 14-16, and 18-20, are rejected under 35 U.S.C. 103(a) as being unpatentable over Jain et al. (J. Med. Chem, 1994).

Jain et al. explicitly describes the use of only molecular surface representation of its three dimensional structure (see abstract) for predicting the biological activities of molecules as described in lines 4 and 39-40, of claim 1. In addition, page 2318, first column, describes selecting "sampling points" on or "near" (1st paragraph) the surface of the molecule (as seen in line 17 of claim 1) for deriving feature values such as steric and polar features (hydrogen bond donor/acceptor features). These features such as the steric features consist of the distance from these points to the van der Waals surface of the molecule; thus suggesting van der Waals energies, and steric factor of claim 1, lines 29-30, and 38, respectively. The polar features concern bonding energies which are thus encompassing electrostatic energies thus suggesting the consideration of electrostatic energies of the molecular surface as seen in line 26 of claim 1. On page 2317, paragraph 4 ("2."), describes the use of neural network map for molecular activity prediction as claimed in claims 14 and 19. Jain et al. describes the consideration of a number and position of sample points (which are at or near the surface) thus evaluating a rate in an area (p. 2327, column 1, paragraph 2) as seen in claims 1 (line 19), 10 (line 3), and 11 (line 3). As such, claims drawn to the use and/or method of molecular reaction characteristic prediction (claims 9-12, 14-15, and 18-20) are motivated by Jain et al.

Claims 1, 4, 5, 7-16, and 18-20, are rejected under 35 U.S.C. 103(a) as being unpatentable over Jain et al. (J. Med. Chem., 1994); and further in view of Lavender et al. (IEEE Comp. Graphics & App., 1992) and Chen et al. (Bio.org. & Med. Chem. Letters, 1998).

Lavender et al. describes the division of the object space into [...] boxes," (p. 72, column 1, paragraph 4) or "component spaces" as in claim 1, lines 9-10. In addition, he continues the description by "retaining for each box only those [primitive surfaces]" later stating in the last paragraph, the only concern being with the surface of the model. Lavender et al. describes on page 76 (column 1, paragraph 1) the selection of "critical points", or probe points, not only on the surface, but also on the boundaries of intersecting surfaces. This consideration of intersecting surfaces described in Lavender et al. is reflected in claims 4 and 5. In the conclusion (p. 76), it is stated that the Voronoi diagram of arbitrary objects "opens the possibility of defining Voronoi diagrams of arbitrary point sets". Thus this shows motivation in the instant application to use the Voronoi diagram in many utilities such as the determination of probe points, probe atoms, or mother points as in claims 1 or 8 (lines 2-6). The Voronoi diagram has many applications to a variety of areas, from finite-element mesh generation to feature recognition. Its "finite collection of distinct points" (p. 69, paragraph 2) is well know and thus can be used in modeling techniques as in Jain et al.

Chen et al. describes the use of a molecular field analysis in a three-dimensional, or spatial dimension, fashion for bioactivity studies (see abstract) as seen in claim 1, lines 5 and 40. In addition, page 1293 (paragraph 3) continues to describe claim 1's use of the "steric and electrostatic contribution" for characterization purposes. The motivation of molecular orbital use as seen in claims 7 and 13, are shown on page 1293 (paragraph 3) in the use of the sp^3 carbon

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probe atom. Chen et al. provided further insights to structure requirements, as in Jain et al.'s three-dimensional structure analysis, by carrying out 3D-QSAR studies using the comparative molecular field analysis (CoMFA) (p.1291, paragraph 1).

No claim is allowed.

Abstract Objection

Applicant is reminded of the proper format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 250 words. It is important that the abstract not exceed 250 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Monika B. Sheinberg, whose telephone number is (703) 306-0511. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst, Tina Plunkett, whose telephone number is (703) 305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

June 4, 2001

Monika B. Sheinberg
Patent Examiner
Art Unit 1631

MB

Ardin H. Marschel
ARDIN H. MARSCHEL
PRIMARY EXAMINER